DISCUSSION OF THE PAPER BY PETER JORDAN: "CHEMOTHERAPY OF SCHISTOSOMIASIS"

FRANCISCO RAMOS-MORALES

Professor and Chairman of the Department of Medicine
University of Puerto Rico Medical School
San Juan, Puerto Rico

I CONGRATULATE Peter Jordan on the beautiful presentation he has made. Professor Jordan has covered the subject very well and, I must say, has expressed the same ideas that I myself hold.

I should like to comment on several aspects of the subject. One is the problem of drug evaluation. Let us remember that we are dealing with human beings and must take all sorts of precautions to protect the welfare of these human volunteers. In the initial phases, one must closely supervise the patient and keep a 24-hour surveillance and observation of dosage on him. Further, one must design a way to detect early side reactions or reactions of toxicity and employ a battery of tests to evaluate abnormalities of the blood and the functions of the heart, kidneys, brain, liver, and other organs. These tests must be performed before, during, and after the period of administration of the drug.

One encounters complications in evaluating the results of the treatment. In different studies that have been done in the past, many different criteria have been used in measuring the main effects of treatment. Many studies last only for a period of perhaps two or three months after the final administration of the drug. Let us remember, however, that there might well be initial tests in which the output of ova is decreased, but that later the female worm that was hurt by the drug might recover, and the production of ova might increase again. Further, if the patient is not followed carefully, it is possible to overlook late effects of the drug; for example, a medication might not be quite as effective as one would like it to be initially, but it might, in the long run—let us say for a period of one year—cause injury to the trematode in such a way as to decrease its productive life. Therefore the patient must be

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followed for at least one year, preferably for a longer time, perhaps for a whole lifetime.

Another complicating factor has been the usual method of evaluation by the egg count. My experience has been mainly with the *mansoni* type by stool examination, and many variables are involved in stool examination. For example, if I take from my clinic 100 patients who have well-known cases, well proved, and I do one stool examination on each, less than 50 per cent of these will be positive on that single stool examination. In the first decade of illness, when the production of ova is highest, three stool examinations can detect about 92 to 93 per cent of the cases. Moreover, in the same patient from one week to another and, many times, from one day to the other, the number of ova that one can recover also is variable. Many times the pretreatment egg count is compared with the posttreatment egg count. We have had a peculiar experience with this comparison. Usually I maintain a group for drug evaluation, and another group in which the treatment of each patient consists merely of a placebo. Twice I recall that in the treated group there was a significant decrease in the number of eggs after therapy, as compared with the number of eggs before treatment in that same patient. And to my surprise, the group receiving placebos showed exactly the same result. If I had had the treatment group alone, I should have attributed the decrease in egg count to medication.

How do I treat patients in relation to available antischistosomal therapy? This is a problem that we find in practice every day. We make the diagnosis and then—what to do? What to recommend for that patient? Remember that we do not have a highly effective drug that would ensure cure, and that many of those whom we treat have side reactions at times: reactions that sometimes lead to complications and death.

It seems that in Puerto Rico things have been changing during the last 15 years. I remember that initially we used to treat every patient in whom the diagnosis was made, and that antimonials were used liberally in the community. Then we gradually encountered more side reactions. I heard of patients who had died in treatment. Fortunately, none of these were my patients. We were also not very satisfied with the effect of treatment. We were afraid to recommend medication to the patients. From my experience with Manson's schistosomiasis, I usually do not recommend treatment for those patients in whom there is

no splenomegaly. That is, I examine the patient and study him; if I do not feel the spleen, I do not use specific treatment, since I have rarely seen severe complications in Manson's schistosomiasis in the absence of an enlarged spleen. Usually in portal hypertension a patient with this disease will have a big spleen. A patient who has pulmonary hypertension will also have a big spleen.

Occasionally splenomegaly may be transitory; in some patients it may disappear. Again, unfortunately, there are patients who develop splenomegaly late; hence a patient who does not have splenomegaly in three or four years might develop it later. Such a patient therefore requires very careful follow-up. Remember, there is usually no immediate need for treatment. Schistosomiasis is a progressive disease that develops slowly. Take your time, study your patient well, decide which drug you would like to use, know its reactions well, take all the precautions necessary to protect the patient, and keep him under constant observation.

Finally I should say, regarding suppressive treatment, that one must be careful about treating large numbers of a population with toxic drugs without close supervision in any attempt to control the disease in the community.